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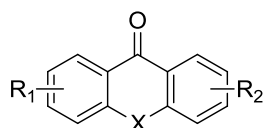
**MICROWAVE-ASSISTED, Yb(OTf)₃/TfOH COCATALYZED
SYNTHESIS OF XANTHONES AND THIOXANTHONES BY
INTRAMOLECULAR FRIEDEL-CRAFTS REACTION UNDER
SOLVENT-FREE CONDITIONS**

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Abstract – An efficient method for the synthesis of biologically interesting xanthenes and thioxanthenes was achieved using Yb(OTf)₃/TfOH as co-catalysts by a microwave radiation-mediated reaction. Both electron-rich and electron-poor substrates could be cyclized in good yields.

Heterocyclic structural elements of the general formula (Figure 1) are common in natural products and molecules of pharmacological interest.^{1,2} The compound of xanthone (9*H*-xanthen-9-one) exhibits a wide range of biological and pharmacological activities, e.g., antibacterial, anti-inflammatory, anticancer, antioxidant, antiulcer and antiviral activities.³⁻⁵ Thioxanthone (9*H*-thioxanthen-9-one) derivatives also exhibit interesting anticancer activities.⁶



X=O xanthenes

X=S thioxanthenes

Figure 1

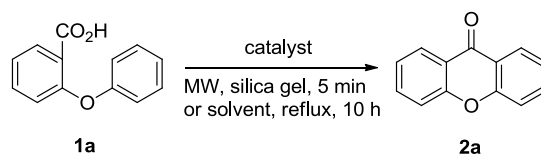
The preparation of such xanthone skeleton typically use benzophenones or diary ethers as intermediate under extremely harsh reaction conditions and/or employed strong acids or toxic metals.⁷⁻⁹ Zhao and Larock have reported a facile one-pot coupling method to synthesize xanthenes and thioxanthenes from

arynes and benzoates in 35-81% yields.¹⁰ η^6 -2-chloro-N,N-diethylbenzamide- η^5 -cyclo-pentadienyl iron hexafluorophosphate was also applied as a common building block for the synthesis of xanthenes and thioxanthenes.¹¹ Nevertheless, most of reported methods are multistep, under harsh reaction conditions or non-atom-economic.

A number of reports have described catalytic Friedel-Crafts acylation reaction using carboxylic acids as acylating reagents.¹²⁻¹⁵ We have recently described the synthesis of 1-azaxanthenes and 1-azathioxanthenes by Yb(OTf)₃/TfOH cocatalyzed intramolecular Friedel-Crafts reaction.¹⁶ To extend the scope of the catalytic system and in an effort to prepare xanthenes and thioxanthenes, we turned our attention to the microwave-assisted Friedel-Crafts reaction. As is known, microwave heating has been widely applied in organic synthesis recently and its benefits have been well documented.^{17,18} Here, we wish to report a new approach based on the microwave-assisted intramolecular Friedel-Crafts reaction for the preparation of xanthenes and thioxanthenes utilizing Yb(OTf)₃/TfOH as co-catalysts under solvent-free conditions.

We started our investigation using 2-phenoxybenzoic acid **1a** as the model substrate. **1a** (4 mmol) and Yb(OTf)₃ (0.2 mmol) were ground with silica gel (0.5 g) under microwave irradiation for 5 min (indicated by TLC), and isolated product **2a** was afforded in 66% yield (entry 5). A blank experiment, in the absence of catalyst gave the unreacted starting material (entry 1). A series of metal triflates were evaluated due to their catalytic activities in Friedel-Crafts reaction.^{16,19} Only 31% yield of **2a** was obtained when using Zn(OTf)₂ (entry 2). Nevertheless, when Cu(OTf)₂ and Bi(OTf)₃ were employed, the product **2a** was generated in 52% and 60% yields, respectively (entries 3 and 4). When 20 mol% of trifluoromethanesulfonic acid (TfOH) was used as the catalyst, the yield of **2a** was slightly improved (entry 6). To our delight, 90% yield of **2a** was obtained when combining 5mol% of Yb(OTf)₃ and 20mol% of TfOH (entry 7). Further optimization using 2mol% of Yb(OTf)₃ and 10mol% of TfOH showed that the yield of **2a** was also in 90% (entry 8). We also compared this reaction with the traditional heating that took 10 h at 165 °C under solvent-free condition, and only 71% yield of **2a** was afforded (entry 9). Effects of solvents on the yields in this reaction were examined and only trace amount of **2a** was detected in the solvent of xylene (entry 11), while in DMF, no reaction was observed (entry 10). Therefore, 2mol% of Yb(OTf)₃ and 10mol% of TfOH as co-catalyst under microwave irradiation for 5 min was chosen as the standard reaction conditions.

With the optimized reaction conditions in hand, we initiated our investigations into the scope of the microwave-assisted, Yb(OTf)₃/TfOH cocatalyzed intramolecular cyclization of various substituted 2-phenoxybenzoic acids and the results are summarized in Table 2. A wide range of 2-phenoxybenzoic acids with both electron-donating (entries 2-5 and 11-13) and electron-withdrawing groups (entries 6-7 and 14-15) afforded the corresponding cyclized products in good to excellent isolated yields. In the case

Table 1. Optimization of reaction conditions for the synthesis of **2a**

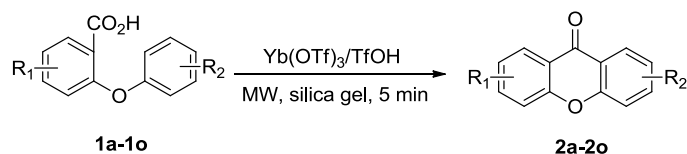
Entry	Catalyst (mol%)	Solvent	Conditions	Yield ^a (%)
1	none	none	MW 5min	N.R. ^b
2	Zn(OTf) ₂ (5)	none	MW 5min	31
3	Cu(OTf) ₂ (5)	none	MW 5min	52
4	Bi(OTf) ₃ (5)	none	MW 5min	60
5	Yb(OTf) ₃ (5)	none	MW 5min	66
6	TfOH(20)	none	MW 5min	78
7	Yb(OTf) ₃ /TfOH(5/20)	none	MW 5min	90
8	Yb(OTf) ₃ /TfOH(2/10)	none	MW 5min	90
9	Yb(OTf) ₃ /TfOH(2/10)	none	165 °C 10 h	71
10	Yb(OTf) ₃ /TfOH(2/10)	DMF	reflux 10 h	N.R.
11	Yb(OTf) ₃ /TfOH(2/10)	xylene	reflux 10 h	trace

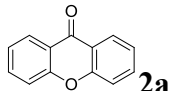
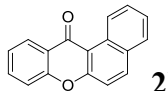
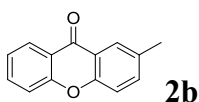
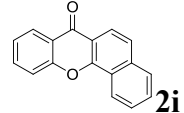
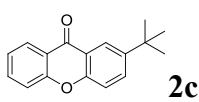
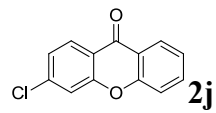
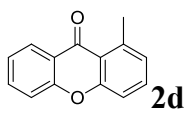
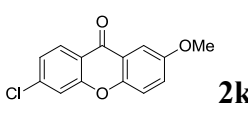
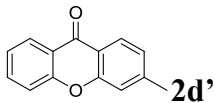
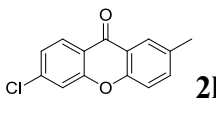
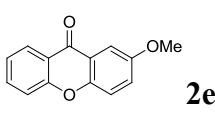
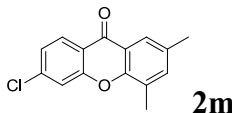
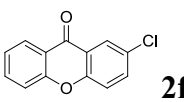
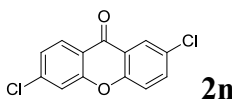
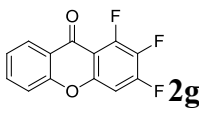
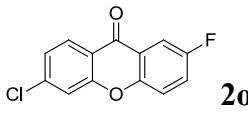
^a yield of isolated product

^b N.R.= no reaction

of *meta*-substituted substrate **1d**, two regioisomeric xanthone products **2d** and **2d'** were obtained in 96% total yield (entry 4). Substrates **1h** and **1i** with a naphthyl moiety also worked well under the same reaction conditions affording 82% and 87% yields of the corresponding tetracyclic xanthone products, respectively (entries 8 and 9). It is important to note that fluoride and chloride groups are tolerated in this process (entries 6-7 and 10-15), which provided access to more structurally diverse xanthone skeletons via metal-catalyzed cross-coupling reactions.²⁰ We were very excited to find that the deactivated substrate **1g** bearing three fluorine atoms on aromatic ring was successfully transformed to **2g** in 73% yield (entry 7).

Table 2. Extension of substrates for the synthesis of xanthenes



Entry	Product	Yield (%)	Entry	Product	Yield (%)
1	 2a	90	8	 2h	82
2	 2b	98	9	 2i	87
3	 2c	91	10	 2j	80
4	 2d	33	11	 2k	77
	 2d'	63	12	 2l	95
5	 2e	79	13	 2m	90
6	 2f	76	14	 2n	76
7	 2g	73	15	 2o	75

The new catalytic system was also successfully utilized for the synthesis of biologically interesting thioxanthenes from corresponding 2-phenylthiobenzoic acids. All of the results are summarized in Table 3. The methyl-, methoxy- and chloro-substituted substrates **3b-3h** have been allowed to react under our usual reaction conditions, and 70-85% yields of the substituted thioxanthenes **4b-4h** have been obtained (entries 2-8). It is noteworthy that chloride-containing thioxanthenes were obtained (entries 4-8) and these products could be subject to facile functionalization *via* various Pd-catalyzed reactions.²⁰ *Para*- and

meta-substituted 2-phenylthiobenzoic acids gave the corresponding products in good yield (entries 6 and 7) whereas a *ortho*-substituted 2-phenylthiobenzoic acid gave the product in a slightly lower yield probably due to the steric hindrance (entry 8).

Table 3. Extension of substrates for the synthesis of thioxanthenes^a

3a-3f $\xrightarrow[\text{MW, 4 min}]{\text{Yb(OTf)}_3/\text{TfOH}}$ **4a-4f**

Entry	Product	Yield (%)	Entry	Product	Yield (%)
1		72	5		73
2		81	6		85
3		79	7 ^b		82
4		70	8		71

^a Reaction condition: Yb(OTf)₃ (2 mol%), TfOH (10 mol%) and **3** (4 mmol) were ground together under microwave irradiation for 4 min.

^b This reaction produced a side product in trace which was not identified.

In summary, we have demonstrated a novel and efficient protocol for the preparation of biologically interesting xanthenes and thioxanthenes by a microwave radiation-mediated reaction using Yb(OTf)₃/TfOH as co-catalysts. Short reaction times, simple reagents, easy and clean work-up and solvent-free conditions are notable advantages of this method and these make this method an attractive and useful alternative to the existing methods for xanthenes and thioxanthenes. Further investigations using this methodology to construct biologically active xanthone containing molecules are underway.

EXPERIMENTAL

All the reactions were carried out in a domestic microwave oven: Galanz P70D20TL-D4 model

(300W-700W) in closed Teflon container. Solid supports: Silica gel (mesh, 200-300). Melting points were determined by Büchi B-540 melting point apparatus and are uncorrected. The IR spectra (KBr pellet) were measured on a Nicolet Avatar-370 spectrometer. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian 400-MHz spectrometer. Mass spectra were obtained on a Thermo Finnigan LCQ-Advantage spectrometer (ESI, APCI) or a Finnigan Trace DSQ spectrometer (EI, CI). HRMS was carried out on an APEX (Bruker) mass III spectrometer.

General Procedure for Synthesis of xanthone 2a

All reactions were performed using a Galanz P70D20TL-D4 microwave oven. A mixture of 2-phenoxybenzoic acid (4 mmol), $\text{Yb}(\text{OTf})_3$ (0.08 mmol), TfOH (0.4 mmol) and dry silica gel (0.5 g) was mixed together in a crucible. Then the mixture was placed in the capped microwave reactor and the crucible was irradiated for 5 min. The reaction was monitored by TLC. At completion of the reaction, the resulting mixture was purified directly by column chromatography [eluent: petroleum/EtOAc (10:1)].

9H-Xanthen-9-one (2a)

White solid. mp 175-176 °C (Lit.,²¹ mp 172-173 °C). IR (KBr): 1656, 1607, 1459, 1345, 1331, 758 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.33 (dd, $J = 8.0, 1.6$ Hz, 2H), 7.74-7.69 (m, 2H), 7.49 (d, $J = 8.4$ Hz, 2H), 7.40-7.35 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ : 176.8, 155.8 (2C), 134.5 (2C), 126.4 (2C), 123.7 (2C), 121.6 (2C), 117.7 (2C). MS (ESI): $m/z = 197$ ($\text{M}^+ + 1$).

2-Methyl-9H-xanthen-9-one (2b)

White solid. mp 122.7-123.2 °C (Lit.,²² mp 122 °C). IR (KBr): 3060, 2917, 1656, 1608, 1476, 1318, 760 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.32 (dd, $J = 8.4, 2.4$ Hz, 1H), 8.09 (s, 1H), 7.71-7.66 (m, 1H), 7.51 (dd, $J = 8.0, 2.0$ Hz, 1H), 7.45 (d, $J = 8.4$ Hz, 1H), 7.38-7.32 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 177.1, 156.1, 154.3, 136.1, 134.7, 133.7, 126.7, 125.8, 123.7, 121.8, 121.5, 118.0, 117.8, 21.2. MS (ESI): $m/z = 211$ ($\text{M}^+ + 1$).

2-(tert-Butyl)-9H-xanthen-9-one (2c)

White solid. mp 111.6-112.5 °C (Lit.,²³ mp 114-115 °C). IR (KBr): 3068, 2970, 2953, 2867, 1658, 1614, 1467, 1320, 761 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.33 (dd, $J = 8.0, 1.6$ Hz, 1H), 8.30 (d, $J = 2.4$ Hz, 1H), 7.77 (dd, $J = 8.8, 2.4$ Hz, 1H), 7.71-7.67 (m, 1H), 7.46 (d, $J = 8.8$ Hz, 1H), 7.42 (d, $J = 8.8$ Hz, 1H), 7.35 (t, $J = 7.2$ Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ : 177.1, 155.8, 154.0, 146.8, 134.6, 132.5, 126.5, 123.5, 122.2, 121.6, 120.9, 117.7, 117.4, 34.8, 31.4 (3C). MS (ESI): $m/z = 253$ ($\text{M}^+ + \text{H}$).

1-Methyl-9H-xanthen-9-one (2d)

White solid. mp 110.3-111 °C (Lit.,²⁴ mp 109.5-110.5 °C) IR (KBr): 2963, 2922, 1655, 1600, 1473, 1344, 763 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 8.25 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.66-7.62 (m, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.33-7.27 (m, 2H), 7.08 (d, *J* = 7.6 Hz, 1H), 2.92 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ: 178.5, 157.2, 154.9, 141.7, 134.0, 133.4, 126.4, 123.4, 122.5, 119.8, 117.2, 115.8, 23.3. MS (ESI): *m/z* = 211 (M⁺+1).

3-Methyl-9H-xanthen-9-one (2d')

White solid. mp 93-95 °C (Lit.,²⁴ mp 98 °C). IR (KBr): 3064, 2923, 1657, 1605, 1464, 1325, 758 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 8.31 (d, *J* = 7.6 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.25 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 2.49 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ: 176.6, 155.9, 146.0, 134.3, 126.4, 126.2, 125.2, 123.5, 121.6, 119.3, 117.7, 117.5, 22.0. MS (ESI): *m/z* = 211 (M⁺+1).

2-Methoxy-9H-xanthen-9-one (2e)

White solid. mp 131.8-132.6 °C (Lit.,²⁵ mp 132-139 °C). IR (KBr): 3033, 2958, 2834, 1649, 1615, 1466, 1317, 758 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 8.33 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.72-7.67 (m, 2H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 9.2 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.31 (dd, *J* = 3.2, 9.2 Hz, 1H), 3.91 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ: 177.0, 156.1, 156.0, 151.0, 134.6 (2C), 126.7, 125.0, 123.8, 122.2, 121.3, 119.5, 118.1, 56.2. MS (ESI): *m/z* = 227 (M⁺+1).

2-Chloro-9H-xanthen-9-one (2f)

White solid. mp 170.3-171.7 °C (Lit.,²⁵ mp 173-173 °C). IR (KBr): 3079, 1663, 1617, 1460, 1316, 757 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 8.31 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.28 (d, *J* = 2.8 Hz, 1H), 7.76-7.70 (m, 1H), 7.65 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.49-7.43 (m, 2H), 7.39 (t, *J* = 7.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ: 175.7, 155.7, 154.1, 134.9, 134.3, 129.4, 126.5, 125.7, 124.0, 122.3, 121.2, 119.5, 117.8. MS (EI): *m/z* (%) = 232 ([M⁺+2], 32), 230 (M⁺, 100), 202 (21), 139 (22).

1,2,3-Trifluoro-9H-xanthen-9-one (2g)

White solid. mp 179- 180 °C. IR (KBr): 3081, 1660, 1646, 1615, 1511, 1469, 1312, 1130, 1066, 761 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 8.26 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.75-7.70 (m, 1H), 7.44-7.37 (m, 2H), 7.14-7.09 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ: 174.1, 155.3, 153.7 (ddd, ¹*J*_{C-F} = 425 Hz, ²*J*_{C-F} = 12 Hz, ³*J*_{C-F} = 5 Hz, 1C), 150.2 (ddd, ¹*J*_{C-F} = 266 Hz, ²*J*_{C-F} = 11 Hz, ³*J*_{C-F} = 6 Hz, 1C), 137.4 (dt, ¹*J*_{C-F} = 349 Hz, ²*J*_{C-F} = 16 Hz, 1C), 135.4, 126.6, 124.9, 121.5, 117.7, 113.3 (d, *J* = 9 Hz, 1C), 110.0 (d, *J* = 7 Hz, 1C).

HRMS (ESI): calcd for $C_{13}H_6F_3O_2 [M+H]^+$: 251.0320, found: 251.0316.

12*H*-Benzo[*a*]xanthen-12-one (2h)

White solid. mp 141-141.7 °C (Lit.,²⁶ mp 143-144 °C). IR (KBr): 3047, 2921, 1643, 1611, 1588, 1467, 1299, 1240, 821, 767, 750 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 10.06 (d, $J = 8.8$ Hz, 1H), 8.41 (d, $J = 7.6$ Hz, 1H), 8.08 (d, $J = 9.2$ Hz, 1H), 7.86 (d, $J = 8.0$ Hz, 1H), 7.75 (t, $J = 8.0$ Hz, 1H), 7.69 (t, $J = 8.0$ Hz, 1H), 7.57 (t, $J = 7.6$ Hz, 1H), 7.51 (d, $J = 8.8$ Hz, 2H), 7.41 (t, $J = 8.0$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 178.0, 157.2, 154.3, 136.3, 133.6, 130.9, 129.9, 129.2, 128.1, 126.7, 126.4, 125.8, 124.0, 123.4, 117.8, 117.3, 114.3. MS (ESI): $m/z = 247 (M^++1)$.

7*H*-Benzo[*c*]xanthen-7-one (2i)

Red solid. mp 159-160 °C (Lit.,²⁶ mp 160 °C). IR (KBr): 3060, 1656, 1608, 1468, 1385, 831, 757 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 8.66 (dd, $J = 7.2, 2.4$ Hz, 1H), 8.39 (dd, $J = 8.0, 2.0$ Hz, 1H), 8.26 (d, $J = 8.8$ Hz, 1H), 7.92 (dd, $J = 7.2, 2.4$ Hz, 1H), 7.78-7.74 (m, 1H), 7.74-7.65 (m, 4H), 7.46-7.41 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 176.5, 155.4, 153.3, 136.2, 134.1, 129.3, 127.8, 126.6, 126.3, 124.2, 123.8, 122.6, 122.2, 121.2, 117.8, 117.3. MS (ESI): $m/z = 247 (M^++1)$.

3-Chloro-9*H*-xanthen-9-one (2j)

White solid. mp 128.2-129.6 °C (Lit.,²⁷ mp 127-128 °C). IR (KBr): 3083, 1677, 1598, 1463, 1424, 938, 754 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 8.31 (dd, $J = 8.0, 1.6$ Hz, 1H), 8.26 (d, $J = 8.8$ Hz, 1H), 7.74-7.70 (m, 1H), 7.51 (d, $J = 2.0$ Hz, 1H), 7.47 (d, $J = 8.4$ Hz, 1H), 7.39 (t, $J = 8.0$ Hz, 1H), 7.33 (dd, $J = 8.4, 1.6$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 176.0, 156.0, 155.7, 140.6, 134.8, 127.9, 126.5, 124.6, 124.1, 121.5, 120.2, 117.9, 117.8. MS (ESI): $m/z = 230 (M^+)$.

6-Chloro-2-methoxy-9*H*-xanthen-9-one (2k)

White solid. mp 165.4-166.4 °C. IR (KBr): 3068, 2974, 2843, 1658, 1596, 1488, 1435, 820, 773 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 8.25 (d, $J = 8.4$ Hz, 1H), 7.65 (d, $J = 3.2$ Hz, 1H), 7.48 (d, $J = 2.0$ Hz, 1H), 7.40 (d, $J = 9.2$ Hz, 1H), 7.32-7.29 (m, 2H), 3.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 175.8, 155.9, 155.8, 150.5, 140.3, 127.8, 124.8, 124.4, 121.8, 119.5, 119.1, 117.7, 105.6, 56.0. HRMS (ESI): calcd for $C_{14}H_{10}ClO_3 [M+H]^+$: 261.0318, found: 261.0316.

6-Chloro-2-methyl-9*H*-xanthen-9-one (2l)

White solid. mp 149-150 °C (Lit.,²⁸ mp 148-148.5 °C). IR (KBr): 3086, 2917, 1660, 1606, 1437, 814, 774 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 8.24 (d, $J = 8.8$ Hz, 1H), 8.07 (s, 1H), 7.52 (dd, $J = 8.4, 2.4$ Hz, 1H),

7.47 (d, $J = 2.0$ Hz, 1H), 7.36 (d, $J = 8.4$ Hz, 1H), 7.31 (dd, $J = 8.8, 2.0$ Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 175.8, 155.8, 153.8, 140.2, 135.9, 133.8, 127.7, 125.74, 124.2, 121.0, 120.0, 117.6, 117.4, 20.8. MS (ESI): $m/z = 245$ ($\text{M}^+ + 1$).

6-Chloro-2,4-dimethyl-9H-xanthen-9-one (2m)

Pale yellow solid. mp 140-142 °C. IR (KBr): 3056, 3007, 2958, 2917, 1657, 1600, 1429, 919, 776 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.23 (d, $J = 8.8$ Hz, 1H), 7.91 (s, 1H), 7.52 (d, $J = 2.0$ Hz, 1H), 7.37 (s, 1H), 7.30 (dd, $J = 8.4, 2.0$ Hz, 1H), 2.49 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 176.0, 155.8, 152.3, 140.2, 137.0, 133.3, 127.8, 126.7, 124.2, 123.4, 121.0, 119.9, 117.8, 20.8, 15.6. HRMS (ESI): calcd for $\text{C}_{15}\text{H}_{12}\text{ClO}_2$ [$\text{M} + \text{H}$] $^+$: 259.0526, found: 259.0523.

2,6-Dichloro-9H-xanthen-9-one (2n)

White solid. mp 219-220 °C (Lit.,²⁹ mp 219-220 °C). IR (KBr): 3092, 1664, 1600, 1437, 1291, 920, 820, 774 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.26-8.22 (m, 2H), 7.66 (dd, $J = 8.8, 2.4$ Hz, 1H), 7.50 (d, $J = 2.0$ Hz, 1H), 7.44 (d, $J = 8.8$ Hz, 1H), 7.35 (dd, $J = 8.4, 2.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ : 175.3, 156.2, 154.4, 141.4, 135.3, 130.3, 128.3, 126.2, 125.3, 122.7, 120.1, 119.9, 118.2. MS (EI): m/z (%) = 266 ([$\text{M}^+ + 2$], 66), 264 (M^+ , 100), 236 (26), 173 (12).

6-Chloro-2-fluoro-9H-xanthen-9-one (2o)

White solid. mp 212-212.7 °C. IR (KBr): 3084, 1665, 1604, 1446, 1294, 1075, 819, 773 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.24 (d, $J = 8.4$ Hz, 1H), 7.94 (dd, $J = 8.0, 2.4$ Hz, 1H), 7.51-7.43 (m, 3H), 7.35 (dd, $J = 8.4, 2.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ : 175.7, 160.2, 156.6 (d, $^1J_{\text{C-F}} = 146$ Hz, 1C), 152.3, 141.3, 128.2, 125.2, 123.4, 123.3 (d, $^2J_{\text{C-F}} = 25$ Hz, 1C), 122.8, 120.1, 119.7, 118.2, 111.8 (d, $^2J_{\text{C-F}} = 23$ Hz, 1C). HRMS (ESI): calcd for $\text{C}_{13}\text{H}_7\text{ClFO}_2$ [$\text{M} + \text{H}$] $^+$: 249.0119, found: 249.0114.

9H-Thioxanthen-9-one (4a)

Yellow solid. mp 219-220 °C (Lit.,³⁰ mp 218-220 °C). IR (KBr): 1644, 1591, 1435, 1320, 731 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.60 (dd, $J = 8.0, 1.2$ Hz, 2H), 7.63-7.59 (m, 2H), 7.57-7.55 (m, 2H), 7.49-7.45 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ : 179.6, 137.10 (2C), 132.1 (2C), 129.7 (2C), 129.0 (2C), 126.1 (2C), 125.8 (2C). MS (EI): m/z (%) = 212 (50), 184 (M^+ , 100), 152 (18), 139 (24).

2-Methyl-9H-thioxanthen-9-one (4b)

Yellow solid. mp 124-124.8 °C (Lit.,²⁵ mp 121-124 °C). IR (KBr): 3059, 2971, 2909, 1633, 1602, 1588, 1438, 1318, 748 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.60 (d, $J = 8.8$ Hz, 1H), 8.41 (s, 1H), 7.60-7.54 (m,

2H), 7.48-7.42 (m, 3H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 180.0, 137.5, 136.5, 134.2, 133.8, 132.2, 129.9, 129.7, 129.7, 129.3, 129.1, 126.2, 126.0, 21.6. MS (EI): m/z (%) = 226 (M^+ , 100), 197 (24).

4-Methoxy-9H-thioxanthen-9-one (4c)

Yellow solid. mp 164.8-165.8 °C (Lit.,³¹ mp 167-169 °C). IR (KBr): 3066, 3000, 2836, 1633, 1595, 1424, 1339, 1265, 735 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.59 (d, $J = 8.0$ Hz, 1H), 8.25 (d, $J = 8.0$ Hz, 1H), 7.64-7.58 (m, 2H), 7.49-7.41 (m, 2H), 7.13 (d, $J = 8.0$ Hz, 1H), 4.04 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 180.0, 154.5, 137.4, 132.3, 130.4, 129.8, 129.1, 127.7, 126.9, 126.4, 126.1, 121.9, 112.4, 56.8. MS (EI): m/z (%) = 242 (11), 226 (M^+ , 100), 197 (35), 165 (14).

4-Chloro-9H-thioxanthen-9-one (4d)

Yellow solid. mp 169-172 °C (Lit.,³² mp 175 °C). IR (KBr): 1650, 1459, 1403, 1318, 735 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.58-8.57 (m, 1H), 8.56-8.55 (m, 1H), 7.71 (dd, $J = 7.6, 1.2$ Hz, 1H), 7.66-7.64 (m, 2H), 7.53-7.49 (m, 1H), 7.44 (t, $J = 8.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ : 179.7, 136.8, 136.7, 132.8, 131.2, 130.4, 130.0, 128.6, 128.5, 127.0, 126.7, 126.4. MS (ESI): $m/z = 247$ (M^++1).

3-Chloro-5-methyl-9H-thioxanthen-9-one (4e)

Pale yellow solid. mp 183.5-184.8 °C. IR (KBr): 3073, 3053, 3013, 1632, 1582, 1380, 1317, 748 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.50 (d, $J = 8.4$ Hz, 1H), 8.47 (d, $J = 8.0$ Hz, 1H), 7.60 (d, $J = 2.0$ Hz, 1H), 7.49 (d, $J = 7.2$ Hz, 1H), 7.42-7.37 (m, 2H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 179.4, 138.7, 137.9, 135.8, 133.8, 133.4, 131.0, 129.1, 127.5, 127.0, 126.8, 125.7, 125.4, 19.4. HRMS (ESI): calcd for $\text{C}_{14}\text{H}_{10}\text{ClOS}$ [$\text{M}+\text{H}$] $^+$: 261.0141, found: 261.0139.

6-Chloro-2-methyl-9H-thioxanthen-9-one (4f)

Pale yellow solid. mp 221-222 °C. IR (KBr): 3074, 3056, 3017, 2912, 1634, 1581, 1401, 1124, 769 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.52 (d, $J = 8.8$ Hz, 1H), 8.39 (s, 1H), 7.54 (d, $J = 2.0$ Hz, 1H), 7.45 (d, $J = 1.2$ Hz, 2H), 7.39 (dd, $J = 8.8, 2.0$ Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 178.9, 138.6, 136.6, 133.7, 133.3, 131.2, 129.4, 128.6, 127.4, 126.6, 125.6, 125.0, 21.3. HRMS (ESI): calcd for $\text{C}_{14}\text{H}_{10}\text{ClOS}$ [$\text{M}+\text{H}$] $^+$: 261.0141, found: 261.0139.

3-Chloro-6-methoxy-9H-thioxanthen-9-one (4g)

Yellow solid. mp 182.5-183.8 °C. IR (KBr): 3073, 3053, 3013, 1632, 1582, 1317, 1102, 748 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 8.49 (d, $J = 8.8$ Hz, 1H), 8.46 (d, $J = 7.2$ Hz, 1H), 7.59 (d, $J = 2.0$ Hz, 1H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.48-7.37 (m, 2H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 179.0, 138.6,

137.9, 135.7, 133.8, 133.3, 131.0, 129.1, 127.4, 126.9, 126.8, 125.7, 125.3, 19.4. HRMS (ESI): calcd for $C_{14}H_{10}ClO_2S$ $[M+H]^+$: 277.0090, found: 277.0085.

3,5-Dichloro-9H-thioxanthen-9-one (4h)

Pale yellow solid. mp 219-221 °C (Lit.,³³ mp 255 °C). IR (KBr): 3081, 1638, 1583, 1402, 1311, 752 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 8.54 (dd, $J = 8.0, 1.2$ Hz, 1H), 8.50 (d, $J = 8.8$ Hz, 1H), 7.72 (dd, $J = 7.6, 1.2$ Hz, 1H), 7.64 (d, $J = 1.2$ Hz, 1H), 7.47-7.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 178.9, 139.6, 138.2, 136.1, 132.9, 131.5, 131.3, 130.5, 128.5, 127.6, 127.0, 126.6, 125.9. MS (ESI): $m/z = 280$ (M^+).

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